

REMARKS

Claims 21, 23-29 and 33-38 are now in the application. The recent personal interview so courteously granted by Examiner Channavajjala is hereby noted with appreciation. Claim 21 has been amended to recite “a concentration of from about 0.05% to 1 %” from claim 33 as mentioned at the interview. Accordingly, claim 33 has been amended. The amendments to the claims do not introduce any new matter.

In addition, the rejection of Claims 21, 23-29, 33-37 under 35 U.S.C. §103(a) as being unpatentable over Goldberg et al (Skin resurfacing utilizing a low-fluence Nd:Y AG laser, J Cutan Laser Ther. 1999;1:23-27) in view of Alster (Combined Laser Resurfacing and Tretinoin Treatment of Facial Rhytides, Cosmetic Dermatology, Volume 10, No. 11, November 1997) in view of Ho et al (Dermatologic Surgery. 1995 December, 21(12),1035-7) and Kye YC (Dermatologic Surgery 1997 October, 23(10): 880-883) was discussed during the interview.

As appreciated by the Examiner, Goldberg does not teach the application of retinoic acid.

The Examiner states that Alster teaches cutaneous laser resurfacing (an ablative process) recently has advanced the treatment of facial rhytides (wrinkles) to provide a youthful look. Combining laser resurfacing with long-term skin care using tretinoin emollient cream provides maximal, long-lasting improvement of facial rhytides.

The Examiner also previously stated that Ho et al. teach laser resurfacing in pigmented skin and skin with acne scars with a CO₂ laser. The method includes: (a) The patients were treated with 0.05% tretinoin, hydroquinone, and desonide cream **nightly for 2-4** weeks prior to the laser treatment (b). The Ultrapulse 50000 CO₂ laser with a setting of 250-450 mJ per pulse, or the Silk Touch flash scanner at the setting of 5-7 W, 0.2-second pulse duration, and 4-mm (M) spot size, is used on the skin; (c) tretinoin, hydroquinone, and desonide and broad spectrum sunscreen is also used postoperatively. Ho discloses the reduction of hyperpigmentation with regular use of tretinoin, hydroquinone, and desonide cream both pre- and postoperatively **along with** use of broad-spectrum sunscreen **after** treatments. The Examiner also previously stated that Kye teaches a

method of resurfacing (an ablative process) pitted facial scars including acne scars, chicken pox scars, and small pox scars, with a pulsed Er:Y AG laser. The method includes: step (a) prior to laser surgery, the patients are treated with 0.05% tretinoin nightly for two to four weeks; step (b) the patient is then treated with Er:YAG laser at a setting of 500mJ/pulse and 3.5-4.5 Watts with a pulse frequency of 7-9 Hz. Kye discloses that after 4-6 laser passes, pinpoint bleeding occurred; step (c) two weeks after laser treatment % tretinoin and 1 hydrocortisone cream is applied for 2-4 weeks. It is respectfully submitted that 0.05% does not read on about 0.1% as asserted by the Examiner.

The Examiner concluded that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the above references and utilize a pre-treatment and post-treatment regimen prior to the laser therapy taught by Goldberg. One would have been motivated to do so since Alster teaches combining laser resurfacing with long-term skin care using tretinoin emollient cream provides maximal, long-lasting improvement of facial rhytides. Therefore, it is prima facie obvious for a skilled artisan to utilize tretinoin to work in conjunction with laser treatment to provide long lasting results.

The secondary references fail to overcome the above deficiencies of Goldberg with respect to rendering unpatentable the present invention. The cited references do not suggest an effective process to produce sustained skin rejuvenation without the type of adverse side effects as achievable according to the present invention. In all of the cited references adverse side effects are reported.

In Alster's method there is substantial trauma to the skin. Within the first 24 hours after treatment the skin turns bright red, swells, and oozes a clear yellowish liquid. Ice packs and ointments or bandages are prescribed for use. The possible side effects include skin lightening or darkening, infection, acne, scarring, and prolonged redness. After the laser surgery the skin is sensitive and each case must be evaluated continuously.

In Ho's method, mentioned is persistent erythema and hyperpigmentation.

In Kye's method there is pinpoint bleeding requiring wet gauze treatment. Erythema occurs and is aggravated by the use of retinoic acid.

In Goldberg's method there is removal of skin cells resulting in erythema. In some cases there is pinpoint bleeding. Golberg states that his procedure is nonablative. Ablation is defined as removal of material from the surface of an object. Thus, Goldberg's method is ablative, although apparently less ablative than those of Alster, Ho, and Kye. Goldberg uses the method of Tankovich as described for hair

removal which explodes carbon particles a sufficient number of times to remove skin and produce erythema.

All of these above methods remove skin and do not leave the epidermis intact as recited in the claims. The prior art teaches that, with laser surgery, some skin must be removed to obtain a beneficial effect on the appearance of the skin.

Tankovich teaches that carbon particles must be exploded a sufficient number of times to remove skin, and that removing skin is necessary to obtain a beneficial effect on the appearance of the skin. Tankovich also teaches that, until that sufficient number of times is achieved, carbon particles can be exploded without removing skin cells. This is shown very clearly in Figures 6 and 7 in US Patent No. 5,423,803, with a corresponding explanation in column 3, lines 30 to 40.

A similar description is shown in Figures 3E and 3F in US Patent No. 6,036,654, with a corresponding explanation in column 4, lines 35 to 45. Thus, the prior art teaches that carbon particles can be exploded on the skin in such a way as to leave the epidermis intact, but being ineffective in treating the skin.

The Applicants submit that in order to make a valid rejection based on a *prima facie* case of obviousness, a combination of references must satisfy the requirements of *KSR International v. Teleflex Inc.* 127 S.Ct. 1727, 82 USPQ 2d. 1385 (2007). Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The Applicants respectfully submit that a *prima facie* case of obviousness has not been established based on this standard.

The position of the USPTO is as follows. Goldberg teaches skin resurfacing using exploding carbon particles but does not teach the use of retinoic acid in combination with the use of exploding particles. To cure this deficiency, the Examiner proposes to combine Goldberg with Alster, Ho, and Kye, wherein Alster, Ho, and Kye teach the use of laser surgery resurfacing in combination with retinoic acid. According to the Examiner, replacing

the laser method of resurfacing with the exploding particle method of resurfacing in Alster, Ho, and Kye would, therefore, be obvious.

The Applicant respectfully disagrees with such a rationale. Some suggestion or motivation to combine the teachings Goldberg with those of Alster, Ho, and Kye must be shown. That Applicant's method leaves the epidermis normal and intact (See specification, page 10, line 12), which must be taken into account in assessing the patentability of the claims. There is no reason to combine Goldberg with Alster, Ho, and Kye because Goldberg does not leave the epidermis intact. Applicant's method of exploding particles, by itself, is ineffective in treating the skin (see Applicant's previously filed Declaration at paragraph 12). Goldberg's method, by itself, as stated in paragraph 18 of Applicant's previously filed Declaration showed modest improvement in superficial skin lines. Applicant stated in her Declaration "When I used this method it was cumbersome, slow, and to many patients painful. " To make the procedure more comfortable to patients, the rate of exploding carbon particles on the skin was speeded up and there was no erythema and the epidermis remained intact. However, there was no significant effect on the skin.

Paragraph 18 of the Declaration further states that using retinoic acid causes skin redness and sensitivity to the sun and that repeated use can cause loss of pigment, painful irritation, dryness, swelling of the skin and contact dermatitis. In addition, paragraph 18 of the Declaration points out minimal exposure to retinoic acid by itself is not effective in producing a sustained improvement in the appearance of skin. Accordingly, the combination of exploding the contaminant particles, such as carbon particles, and intermittent retinoic acid results in an unexpected remarkable improvement in the appearance and condition of skin. As stated in paragraph 18 of the Declaration, Applicant has been using this method of skin rejuvenation since 2003 with great success. Applicant's method and Goldberg's method are, thus, not the same.

Combining Goldberg with Alster, Ho, and Kye does not provide a method for combining retinoic acid with a method which leaves the epidermis intact and which, by itself, is ineffective in treating the skin. One of ordinary skill in the art would know that exploding particles on the skin while leaving the epidermis intact would be ineffective in

treating the skin (see paragraph 18 of the Declaration). One of ordinary skill in the art would not be motivated to combine a method ineffective in treating the skin with retinoic acid, especially with a retinoic acid treatment which is ineffective by itself, which is the case in Applicant's method (see Applicant's declaration previously filed).

The combination of references does not suggest a reasonable expectation of success of effective treatment of the skin by combining a method of exploding particles on the skin which leaves the epidermis intact and which, by itself, is ineffective, with application of retinoic acid. There also is no reasonable expectation of success when the dosing of retinoic acid by itself is ineffective.

Also, the combination of references do not teach or suggest the limitation in claim 25 wherein exploding a contaminant on the surface of the skin of the face with laser light is completed within about 4 minutes. It is inherent in such a limitation that the exploding of particles by the present method would be ineffective in treating the skin by itself, and one of ordinary skill in the art would know this (see Applicant's previously filed declaration). The combination of references do not teach or suggest the limitation of amended claim 33 that retinoic acid is applied topically without producing side effects.

It is well established law that secondary considerations may be used to show that a claim rejected under 35 U.S.C. § 103(a) was not obvious. The courts may look to considerations in determining the obviousness of an invention that include long-felt but unresolved need, failed attempts by others, initial skepticism, subsequent praise, commercial success, and copying by others. *Graham v. John Deere Co.*, 383 U.S. 1 (1966). Secondary indicia of non-obviousness, such as the evidence concerning, among others, unexpected results, must be considered whenever obviousness is an issue. The Applicant respectfully directs the Examiner's attention to the evidence of such secondary consideration as unexpected results which clearly demonstrate that claim 21 is patentably non-obvious over the combination of cited references, and requests the Examiner to consider this evidence. Such evidence can be found directly in the instant application.

The specification on page 9, lines 7-10 state:

In the next steps 42 and 43 a laser beam is scanned over the area treated with the activating solution so as to clean substantially all of the mixture from the skin surface by exploding or fracturing the carbon or graphite particles in the oil. This scanning process takes from about 2 to 10 minutes to complete on the face, usually about 4 minutes.

On page 3, lines 9-10 the specification further states: An advantage of the present invention is the production of a chronic wound in the high dermis with no damage to the epidermis.

On page 10, line 12, the specification further states: Furthermore, this has been accomplished leaving the epidermis intact and normal.

Applicant states in her Declaration that a person of ordinary skill in the art would know that exploding the carbon particles to complete the process on the face within about four minutes, leaving the epidermis intact, undamaged, and normal, would require exploding the carbon particles insufficiently to produce any cosmetic or beneficial effect by itself. One of ordinary skill in the art would not reasonably expect the result of skin rejuvenation and improved appearance of the skin by further adding intermittent topical application of retinoic acid to this process of exploding particles on the skin of the face. The prior art would not reasonably predict such a result because there is nothing in the prior art that teaches or suggests that combining retinoic acid with an exploding particle method which by itself is ineffective in treating the skin would produce skin rejuvenation. It is submitted that the results from adding retinoic acid to the skin in combination with exploding particles on the skin, which by itself is ineffective in treating the skin, to produce sustained rejuvenation of the skin unquestionably qualify as unexpected. Such results would also not be reasonably predicted.

The Examiner has indicated that the specification is not enabling to one of ordinary skill in the art. Applicant respectfully disagrees and provides a declaration stating the reasons why one of ordinary skill in the art would have no difficulty in practicing the invention as claimed based upon the disclosures in the specification. The parameters for producing the necessary laser light are described in sufficient detail in the specification and in the Tankovich prior art (US Patent Nos. 5,423,803 and 6,036,684). Although the Tankovich prior art describes several methods for applying the laser light to carbon particles, there is only one method disclosed in the Tankovich prior art that describes exploding carbon particles in such a way that skin cells are not removed by the process and the epidermis remains intact, as discussed above. This method is described in no uncertain terms in Figures 6 and 7 in US Patent No. 5,423,803, with a corresponding explanation in column 3, lines 30 to 40, and in Figures 3E and 3F in US Patent No. 6,036,684, with a corresponding explanation in column 4, lines 35 to 45. One of ordinary skill in the art

would have no problem identifying this method and applying it. The specification states that "Although the photomechanical laser process of Tankovich is considerably safer than the standard photothermal laser treatments and leaves the epidermis intact, this photomechanical laser process is relatively ineffective in treating the skin and has not been commercially successful." The only method in the Tankovich prior art that is ineffective in treating the skin is the one referenced above (Figures 6 and 7 in US Patent No. 5,423,803, with a corresponding explanation in column 3, lines 30 to 40, and in Figures 3E and 3F in US Patent No. 6,036,684, with a corresponding explanation in column 4, lines 35 to 45). Based upon the disclosures in the specification cited above:

In the next steps 42 and 43 a laser beam is scanned over the area treated with the activating solution so as to clean substantially all of the mixture from the skin surface by exploding or fracturing the carbon or graphite particles in the oil. This scanning process takes from about 2 to 10 minutes to complete on the face, usually about 4 minutes.

It should be kept in mind that for purposes of incorporation by reference, those aspects of the incorporated reference that might be inconsistent with the explicit disclosure and/or would adversely effect the objectives of the present invention are understood by those skilled in the art as not being incorporated.

On page 3, lines 9-10 the specification further states: An advantage of the present invention is the production of a chronic wound in the high dermis with no damage to the epidermis. On page 10, line 12, the specification further states: Furthermore, this has been accomplished leaving the epidermis intact and normal.

To further demonstrate the efficacy of the present invention is a further Declaration by the inventor, which presents the results achieved from treating patients according to the present invention.

One of ordinary skill in the art would have no problem understanding that the laser light of the present invention is applied only sufficiently to explode the particles without damaging the epidermis because it is inherent in the method. Knowing that the object is to explode the carbon particles without damaging the epidermis, it is then easy for one of ordinary skill in the art to know how much time to expose the particles to the laser. That amount of time is that which explodes the particles but does not affect the epidermis. Further guidance is provided in the specification by the description that "This scanning process takes from about 2 to 10 minutes to

complete on the face, usually about 4 minutes" (page 9, lines 7-10), and "A single treatment of the skin of the face can be completed within four minutes" (page 4, lines 3-4). One of ordinary skill in the art would also know that this method, by itself, of exploding the carbon particles would not produce an effect on the epidermis because it is inherent in the method. This is in addition to knowing that Tankovich teaches only one procedure of exploding carbon particles that does not remove skin from the epidermis.

However, the cosmetic benefit is attained when Applicant's exploding carbon particle method (which does not remove the skin) is combined with topical retinoic acid. What applicant discovered, and which was not known in the prior art, is that the combination of an exploding particle method (which stimulates collagen production selectively in the high dermis and which leaves the upper dermis intact) with topical retinoic acid produces a sustained elevation of collagen in the high dermis. It is this increase production of collagen in the high dermis, just beneath the epidermis, which produces a skin resurfacing effect, without any loss of epidermal skin, and without the need to remove epidermal skin. This result was not predictable from the prior art and was unexpected. There is nothing in the prior art to suggest or motivate one to use topical retinoic acid with an exploding particle method that does not remove stratum corneum or which leaves the epidermis intact. Therefore, applicants method as claimed in the amended claims it's not obvious in view of the cited prior art.

The methods disclosed in the cited prior art to resurface the skin do not leave the epidermis intact and undamaged. Applicant's method can be used repeatedly throughout a patient's lifetime without damaging the skin to produce a sustained improvement in the appearance of the skin. The prior art methods disclosed in the cited references cannot be used repeatedly throughout a patient's lifetime without damaging the skin, even if topical retinoic acid is applied.

In view of the above, consideration and allowance are respectfully solicited.

In the event the Examiner believes another interview might serve in any way to advance the prosecution of this application, the undersigned is available at the telephone number noted below.

The Office is authorized to charge any necessary fees due with this paper to Deposit Account No. 22-0185, under Order No. 30042-00001-US from which the undersigned is authorized to draw.

Dated: July 14, 2010

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